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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/087,082	02/28/2002	Wolfgang Dietmaier	1803-0330-999	3192

7590 10/20/2003  
PENNIE & EDMONDS LLP  
1155 Avenue of the Americas  
New York, NY 10036

EXAMINER

CHUNDURU, SURYAPRABHA

ART UNIT	PAPER NUMBER
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1637

DATE MAILED: 10/20/2003

15

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

10/087,082

Applicant(s)

DIETMAIER ET AL.

Examiner

Suryaprabha Chunduru

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 14 July 2003.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1 and 3-9 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1 and 3-9 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All   b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)                      4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)                      5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_                      6) ☐ Other: \_\_\_\_\_

**DETAILED ACTION**

1. Upon reconsideration of request for withdrawal of improper finality, the finality of the previous office action is withdrawn herein.
2. Applicants' response to the office action (Paper No. 13) filed on July 14, 2003 has been considered. Claims 1, 3-9 are pending in this application and are reconsidered for examination.
3. Terminal Disclaimer (Paper No. 14) filed on July 14, 2003 has been entered and considered.

***Response to arguments***

4. Applicants' response to the office action (Paper No. 13) is fully considered and found persuasive.
5. With reference to the rejection made in the previous office action under obviousness-type double patenting, the rejection is withdrawn in view of the terminal disclaimer (Paper No. 14).
6. With reference to the rejection made under 35 USC 102(b), Applicant's arguments have been fully considered and the rejection is withdrawn in view of the arguments (Paper No. 13).
7. With reference to the rejection made under 35 USC 103(a), Applicant's arguments have been fully considered and the rejection is withdrawn in view of the arguments (Paper No. 13).

**New Grounds of Rejections**

***Claim Rejections - 35 USC § 112***

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 4 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the

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invention. Claim 4 recites dependency on canceled claim 2, which makes the claim indefinite and unclear because the meets and bounds of the claim are unclear.

***Claim Rejections - 35 USC § 102***

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 3-6 are rejected under 35 U.S.C. 102(b) as being anticipated by Ando et al. (J Clin Microbiol., Vol. 35, No.3, pages 570-577, 1997).

Ando et al. teach a method of claim 1, for the amplification of nucleic acid fragments from a sample (see page 571, column 2, paragraphs 1-3), said method comprises first (reverse transcription) and second (PCR) amplification reactions (see page 571, column 2, paragraph 3, page 573, Fig. 1), wherein said first amplification is carried out using completely randomized primers (see page 571, column 2, paragraph 2, table 2) and said second amplification reaction is carried out using specific primers (see page 571, tables 1 and 2); and said first and second amplification reactions were carried out using the same mixture of at least two DNA polymerases, at least one of which possesses 3'-5' exonuclease activity (see page 572, column 1, lines 1-17);

With regard to the claim 3 and 5, Ando et al. teach that said mixture of DNA polymerases comprises a DNA polymerase without 3'-5' exonuclease activity (Taq DNA polymerase) and a DNA polymerase with 3'-5' exonuclease activity (pwo DNA polymerase) (see page 572, column 1, lines 1-17, page 576, column 2, lines 5-13);

With regard to claims 4 and 6, Ando et al. teach that the sample comprises a pool of cDNAs (see page 571, column 1, paragraph 1, column 2, paragraph 1, page 575, column 1, paragraph 4); sample comprises stool specimen, which comprise various viral cells (see page 571, column 1, paragraph 1, column 2, paragraph 2). Thus the disclosure of Ando et al. meets the limitations in the instant claims.

***Claim Rejections - 35 USC § 103***

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

A. Claims 7-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ando et al. (J Clin Microbiol., Vol. 35, No.3, pages 570-577, 1997) in view of von Eggeling et al. (Hum Genet., Vol. 99, pp. 266-270, 1997).

Ando et al. teach a method of claim 1, for the amplification of nucleic acid fragments from a sample (see page 571, column 2, paragraphs 1-3), said method comprises first (reverse

transcription) and second (PCR) amplification reactions (see page 571, column 2, paragraph 3, page 573, Fig. 1), wherein said first amplification is carried out using completely randomized primers (see page 571, column 2, paragraph 2, table 2) and said second amplification reaction is carried out using specific primers (see page 571, tables 1 and 2); and said first and second amplification reactions were carried out using the same mixture of at least two DNA polymerases, at least one of which possesses 3'-5' exonuclease activity (see page 572, column 1, lines 1-17). However, Ando et al. did not teach treating the sample cells with proteinase K.

Von Eggeling et al. teach a method for detecting length polymorphisms in single nucleated cells, wherein von Eggeling et al. teach that the method comprises treating the sample of cells with Proteinase K, prior to the two thermocyclic amplification reactions (see page 267, column 1, paragraph 2).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the method for amplification of nucleic acid fragments as taught by Ando et al. with the method of lysing nucleated cells prior to PCR as taught by von Eggeling et al. which is applicable to inhibit nuclease contamination of nucleic acids because von Eggeling et al. states that 'for the purposes high sensitivity PCR, especially in PEP, precautions have to be taken to minimize contamination, which involves the physical separation of pre- and post-PCR procedures' (see page 267, column 2, paragraph 2). An ordinary practitioner would have been motivated to combine the method of Ando et al. with the method of von Eggeling et al. to include the limitation (treating the sample with proteinase K) in order to achieve the expected advantage of developing a high sensitive amplification method for the analysis of nucleic acids.

B. Claim 9 is rejected under 35 U.S.C. 103(a) as being unpatentable over Ando et al. (J Clin Microbiol., Vol. 35(3), 1997) in view of Casas et al. (Biotechniques, Vol. 20(2), pp 219-225, 1996).

Ando et al. teach a method of claim 9, for the amplification of nucleic acid fragments from a sample (see page 571, column 2, paragraphs 1-3), said method comprises first (reverse transcription) and second (PCR) amplification reactions (see page 571, column 2, paragraph 3, page 573, Fig. 1), wherein said first amplification is carried out using completely randomized primers (see page 571, column 2, paragraph 2, table 2) and said second amplification reaction is carried out using specific primers (see page 571, tables 1 and 2); and said first and second amplification reactions were carried out using the same mixture of at least two DNA polymerases, at least one of which possesses 3'-5' exonuclease activity (see page 572, column 1, lines 1-17). However Ando et al. did not teach primer extension at increased temperatures in at least some successive amplification cycles.

Casas et al. teach a method of claim 9, for amplification of nucleic acid fragments from a sample, said method comprises first (primer-extension preamplification) and second (gene-specific amplification) thermocyclic amplification reactions (see page 219, column 2, paragraph 2, page 220, column 2, paragraph 1), wherein the method comprises increase in temperature in at least some successive amplification cycles, that is each cycle consisted of 1-min-denaturation step at 92<sup>0</sup> C, 2-min annealing step at 37<sup>0</sup> C, with a ramping step of 10s / 1<sup>0</sup> C, to 55<sup>0</sup> C, , and a 4-min polymerase extension step at 55<sup>0</sup> C (see page 220, column 3, paragraph 1).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the method of amplification of nucleic acid fragments as taught

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by Ando et al. with the method of primer extension cycles as taught by Casas et al. which is applicable to amplify long regions of a genome because Casas et al. states that "primer-extension preamplification (PEP) involving repeated primer extensions, is an in vitro procedure developed to duplicate a large fraction of the genome from a limited amounts of DNA" (see page 576, column2, paragraph 1). An ordinary practitioner would have been motivated to combine the method of Ando et al. with the method of Casas et al. et al. by including the limitation of primer extension cycles as taught by Casas in order to achieve the expected advantage of developing a high sensitive PEP-PCR method for the analysis of whole genome containing samples.


### *Conclusion*

No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Suryaprabha Chunduru whose telephone number is 703-305-1004. The examiner can normally be reached on 8.30A.M. - 4.30P.M, Mon - Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 703-308-1119. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and - for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

  
Suryaprabha Chunduru  
October 15, 2003

  
**JEFFREY FREDMAN**  
**PRIMARY EXAMINER**